

## **REMARKS**

Claims 20-41 and 43-55 are pending in the application. Claims 20-38 are withdrawn from consideration by the Examiner as being directed to non-elected inventions. Claims 39, 45, 46, and 53 are canceled herein without prejudice or disclaimer. Claims 40, 41, and 44 are amended herein for clarity to more particularly define the invention. New claim 56 is added herein. Support for these amendments and new claim can be found throughout the specification and in the language of the original claims, as set forth below. It is believed that no new matter is added by these amendments and new claim and their entry and consideration are respectfully requested. In light of these amendments and new claim and the following remarks, applicant respectfully requests reconsideration of this application and allowance of the pending claims to issue.

### **I. Objection to the specification**

The Action states that the specification is objected to because Tables 1, 2 and 3 contain sequences that are set forth in the Sequence Listing that are not identified by SEQ ID NOs.

The specification is amended herein on pages 18, 19 and 20 to replace Tables 1, 2, and 3 with tables reciting the SEQ ID NO for each sequence included in the tables, thereby obviating this objection. Therefore, applicant respectfully requests the withdrawal of this objection.

### **II. Objection to the claims**

The Action states that claim 44 is objected to because it depends from claim 42 and claim 42 is canceled.

Claim 44 is amended herein to depend from claim 40, thereby obviating this objection. Therefore, applicant respectfully requests its withdrawal.

### **III. Rejection under 35 U.S.C. § 112, second paragraph**

The Action states that claims 39-41 and 43-52 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

As an initial point claims 39 and 53 are canceled herein without prejudice. Accordingly, the rejections under 35 U.S.C. §112, second paragraph, are mooted with respect to these claims.

A. The Action alleges that claims 39-41 and 43-52 are indefinite over the recitation of the phrase "unmodified nucleic acid." Applicant respectfully traverses this rejection.

Applicant respectfully points out that, it is well settled that "a patent need not teach, and preferably omits, what is well known in the art". *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986) and MPEP 2164.01. It is further noted that claims 39-41 and 43-52 recite "unmodified nucleotides." Applicant respectfully submits that one of skill in the art would readily recognize that unmodified nucleotides are those that are natural, i.e., adenine, guanine, cytosine, thymine and uracil. That this is the meaning given the phrase "unmodified nucleotide" is clear from a reading of the specification, for example, at least on page 3, lines 28-32; on page 6, lines 12-17 and lines 24-30, and on page 6, line 31, to page 7, line 3.

Accordingly, applicant submits that the phrase "unmodified nucleotides" as recited in claims 39-41 and 43-52 is a commonly used and well known term of art and therefore, applicant respectfully requests that the rejection be withdrawn.

B. The Action further alleges that claims 40-41 and 43-52 are indefinite over the recitation of the phrase "said probe allowing the lowering of the possible opening of the stem loop structure of the molecular beacon." Specifically, the Action alleges that the phrase is considered indefinite because the claims do not define what constitutes the "possible opening" and that it is also unclear how the probe itself can allow for lowering of its own stem loop structure as opposed to the inclusion of a modified nucleotide analog in the probe resulting in the lowering of the opening of the stem loop structure.

Claim 40 as presented herein recites that said probe has better stability and does not open spontaneously in the presence of contaminants present in an amplification enzyme mixture comprising said molecular beacon probe as compared to a molecular beacon probe without said stem. Claim 41 as presented herein recites that the spontaneous opening of the probe in the presence of contaminants present in an amplification enzyme mixture comprising said molecular beacon probe is lowered as compared to a molecular beacon probe without said stem. Support for these amendments can be found in the specification, for example, at least on page 7, line 25, through page 8, line 2.

Accordingly, claims 40-41 and claims dependent thereon no longer recite the phrase "said probe allowing the lowering of the possible opening of the stem loop structure of the molecular beacon." Therefore, applicant submits that these claims are now clarified and respectfully request that this rejection be withdrawn.

C. The Action further alleges that there is insufficient antecedent basis for the recitation of the "amplification enzyme mixture" in claim 40. The Action additionally states that it isn't clear as to what is intended to be the relationship between the probe and the enzyme mixture and there it is unclear how this phrase is intended to further limit the claim.

As noted above, claim 40 recites that said probe has better stability and does not open spontaneously in the presence of contaminants present in an amplification enzyme mixture comprising said molecular beacon probe as compared to a molecular beacon probe without said stem. Thus, applicant has addressed the issue of antecedent basis and further makes clear the relationship between the amplification mixture and the probe.

Accordingly, the concerns of the Examiner having been addressed, applicant respectfully requests the withdrawal of this rejection.

**D.** The Action further alleges that claims 40, 45, 47, 49, and 51 are indefinite for the recitation of the phrase in claim 40 of "having an affinity increasing modification is selected from the group consisting of...." The Action states that this phrase should clarify that the probe stem comprises one or more nucleotides and the one or more nucleotides are selected from the group consisting of 2'-O-derivatized nucleotides, a locked nucleic acid and a peptide nucleic acid.

Claim 40 as presented herein recites one or more nucleotides or nucleotide analogues having an affinity increasing modification, wherein said one or more nucleotides or nucleotide analogues are selected from the group consisting of a 2'-O-derivatized nucleotide, a locked nucleic acid, and a peptide nucleic acid.

Accordingly, applicant submits that claim 40 is clarified and respectfully requests that this rejection be withdrawn.

**E.** The Action further alleges that claims 41, 43, 46, 48, 50 and 52 are indefinite for the recitation in claim 41 of the phrase "and/or." Specifically, the Action states that that it is unclear if the probe stem has one or more unmodified nucleotides (line 8) and then additional one or more unmodified nucleotides (line 11).

Claim 41 as presented herein recites a molecular beacon probe comprising a stem and a loop, wherein said loop comprises: one or more nucleotides and/or nucleotide analogues that have an affinity increasing modification, and one or more unmodified nucleotides; and said stem comprises: one or more 2'-O-methyl nucleotides, and one or more unmodified nucleotides. Thus, claim 41 clearly recites that the one or more unmodified nucleotides in line 8 refers to the loop of the molecular beacon probe and the one or more unmodified nucleotides in line 11 refers to the stem of the molecular beacon probe.

Accordingly, applicant submits that claim 41 is clarified and therefore respectfully requests the withdrawal of this rejection.

F. The Action further alleges that claims 41, 43, 46, 48, 50 and 52 are indefinite for the recitation in claim 41 of the phrase "said probe allowing the lowering of the effect of sequence variations in a nucleic acid analyte."

Claim 41 as presented herein recites that the sensitivity of said probe to polymorphisms in the target nucleic acid sequence is lowered as compared to a molecular beacon probe without said loop. Support for this amendment can be found in the specification, for example, at least on page 11, lines 15-23.

Accordingly, applicant submits that claim 41 is clarified and therefore respectfully requests the withdrawal of this rejection.

#### **IV. Rejection under 35 U.S.C. § 102**

The Action states that claims 39-41 and 43-52 are rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Becker (U.S. Patent Publication No 2003/0105320) as evidenced by Majlessi (*Nucleic Acids Res.* 25:2224-2229 (1998)).

As an initial point, claims 39 and 53 are canceled herein without prejudice. Accordingly, this rejection is mooted with respect to these claims.

Case law very specifically holds and the M.P.E.P. states that a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, the identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Additionally, anticipation under 35 U.S.C. § 102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention. *Apple Computer Inc. v. Articulate Systems Inc.* 57 USPQ2d 1057, 1061 (Fed. Cir. 2000). It is clear that Becker (as evidenced by Majlessi et al.) fails to anticipate claims 39-41 and 43-52 of the

present invention because the cited reference fails to teach each and every limitation of the methods set forth in these claims.

Claim 40 as presented herein recites a molecular beacon probe, comprising: a stem comprising one or more nucleotides or nucleotide analogues having an affinity increasing modification, wherein said one or more nucleotides or nucleotide analogues are selected from the group consisting of a 2'-O-derivatized nucleotide, a locked nucleic acid, and a peptide nucleic acid, and one or more unmodified nucleotides, wherein each base pair of said stem comprises no more than one 2'-O-methyl nucleotide. Claim 41 as presented herein recites a molecular beacon probe comprising a stem and a loop, wherein said loop comprises: one or more nucleotides and/or nucleotide analogues that have an affinity increasing modification, and one or more unmodified nucleotides; and said stem comprises: one or more 2'-O-methyl nucleotides, and one or more unmodified nucleotides, wherein each base pair of said stem comprises no more than one 2'-O-methyl nucleotide. Support for these amendments can be found in the original claims, for example, at least in claims 45 and 46.

Thus, the molecular beacon probe of the present invention comprises a loop comprising both modified and unmodified nucleotides and/or a stem with both modified and unmodified nucleotides. Further, none of the 2'-O-methyl nucleotides in the stem of the probe of the present invention are base paired with another 2'-O-methyl nucleotide (i.e., each base pair of said stem comprises no more than one 2'-O-methyl nucleotide). In contrast, Becker teaches a molecular beacon probe wherein the loop is comprised entirely of 2'-O-methyl nucleotides and the stem comprises 2'-O-methyl nucleotides and unmodified nucleotides in which all 2'-O-methyl nucleotides in the stem are based paired only with other 2'-O-methyl nucleotides. Thus, Becker fails to teach each and every limitation of the claimed invention.

Accordingly, applicant submits that the present invention is not anticipated by Becker and respectfully requests that this rejection under 35 U.S.C. § 102(e) be withdrawn.

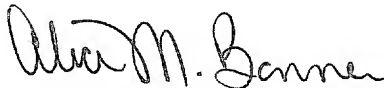
## V. New Claims

New claim 56 is added herein. Support for this claim can be found in the language of the original claims and throughout the specification. Thus, no new matter is believed to be added by this new claim. Claim 56 is believed to be free of the pending rejections for the same reasons set forth above explaining why claims 40-41, 43-52, and 54-55 are free of the pending rejections. Accordingly, its entry and allowance are respectfully requested.

The points and concerns raised in the Action having been addressed in full herein, it is respectfully submitted that this application is in condition for allowance, which action is respectfully requested. Should there be any remaining concerns, the Examiner is encouraged to contact the undersigned attorney by telephone to expedite the prosecution of this application.

The Commissioner is authorized to charge Deposit Account No. 50-0220 in the amount of \$130.00 for a one month extension of time. This amount is believed to be correct. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,



Alice M. Bonnen

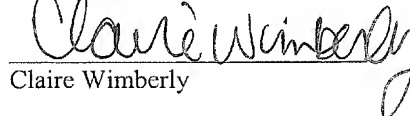
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#### CERTIFICATION OF ELECTRONIC TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on January 12, 2009

  
Claire Wimberly